

REMARKS

Claims 1-23 were pending in this application. All claims have been rejected on the alleged grounds of indefiniteness, anticipation, and obviousness. To expedite prosecution without acquiescing to the Examiner's arguments, Applicants have canceled claims 18-20 without prejudice and have added new claims 24-26. The newly added claims are supported in the specification, for example at page 4, lines 18-24, and in the claims as originally filed. No new matter has been added. Applicants have also amended claim 1 to better define the invention. Thus, claims 1-17 and 21-26 are pending.

Claim Rejections under 35 U.S.C. §§ 101 and 112

The Examiner rejected claims 18-20 under 35 U.S.C. § 112, as allegedly being indefinite. The Examiner also rejected claims 18-20 under 35 U.S.C. § 101, as improper process claims. To expedite prosecution without acquiescing to the Examiner's arguments, Applicants have canceled claims 18-20, and added new claims 24-26. Claims 24-26 relate to methods of drug delivery comprising administering the hydrogel compositions of claim 1, and are proper method claims. Thus, Applicants respectfully request that these rejections be withdrawn.

Claim Rejections Under 35 U.S.C. § 102

The Examiner rejected claims 1-5, 7-10 and 13 under 35 U.S.C. § 102(b), as allegedly being anticipated by Okihara *et al.* (*J. Macromol. Sci. Phys.* B30: 119-140 (1991)). The Examiner alleged that Okihara discloses a stereocomplex mixture comprising equimolar amounts of poly(L-lactide) and poly(D-lactide), which inherently forms a hydrogel. Applicants must respectfully disagree.

Anticipation requires that the prior art reference disclose each element of the claimed invention. The hydrogels of the presently claimed invention comprise a mixture of water soluble or water dispersible polymers in an aqueous system comprising noncovalent oligomerized monomers

of opposite chiralities. (See Specification at page 4, lines 1-24). In contrast, Okihara describes the crystal structure of a poly(L-lactide) and poly(D-lactide) stereocomplex.

As a preliminary matter, a hydrogel is a colloidal gel where water is the dispersion medium. Unlike a hydrogel, the stereocomplexes described in the Okihara reference are crystalline and do not comprise water soluble or water dispersible polymers in an aqueous system. Thus, contrary to the Examiner's assertions, the Okihara stereocomplexes are entirely different compositions from the presently claimed invention, and thus, would not inherently form a hydrogel. Because Okihara does not disclose hydrogels, let alone hydrogels comprising a mixture of water soluble or water dispersible polymers in an aqueous system comprising noncovalent oligomerized monomers of opposite chiralities, the claims are not anticipated. Applicants respectfully request that this rejection be withdrawn.

The Examiner also rejected claims 1-10, 14 and 21-23 under 35 U.S.C. § 102(b), as allegedly being anticipated by Hennink *et al.* (WO 98/00170). The Examiner alleged that Hennink discloses a biodegradable hydrogel containing hydrolysable bonds and consisting of two interpenetrating networks interconnected to one another. The hydrogel is prepared by radical polymerization, where increasing the degree of substitution yields a more cross-linked network. Applicants must respectfully disagree, and address the Examiner's rejection in view of amended claim 1.

As previously indicated, the hydrogels of the presently claimed invention comprise a mixture of water soluble or water dispersible polymers in an aqueous system comprising noncovalent oligomerized monomers of opposite chiralities. In contrast, the Hennick hydrogel compositions contain hydrolysable bonds consisting of two interpenetrating networks interconnecting to one another. The hydrogels are prepared by synthesizing spacers which contain at least one crosslinkable group and at least one hydrolytically labile group; coupling such spacers to a waters-soluble polymer, and crosslinking the polymers. (See WO 98/00170, page 8, lines 2-9).

Thus, the Hennink hydrogels are intermolecularly linked through covalent linking groups. For example, the Hennink hydrogels are based on a polymer covalently crosslinked with methacrylate units. Other crosslinking units are acrylate units, vinyl ethers and vinyl esters, as well as other known crosslinking units in the art. (See WO 98/00170, page 6, lines 23-27). Because Hennick does not disclose a hydrogel comprising a mixture of non-covalent oligomeric groups of opposite chiralities, the claims are not anticipated. Applicants therefore respectfully request that this rejection be withdrawn.

Claim Rejections Under 35 U.S.C. § 103

The Examiner rejected claim 11 under 35 U.S.C. § 103(a) as allegedly being unpatentable under Hennink et al. (WO 98/00170). The Examiner alleged that Hennink teaches that increasing the degree of substitution yields a more cross-linked network. Applicants must respectfully disagree, and address the Examiner's rejection in view of amended claim 1.

Hennink fails to teach or suggest claim 1, from which claim 11 depends from. As previously indicated, the Hennink hydrogels are intermolecularly linked through covalent linking groups. There is no suggestion or motivation to modify intermolecularly crosslinked polymers to teach hydrogels comprising non-covalent oligomeric groups, let alone non-covalent oligomeric groups of opposite chiralities. Because independent claim 1 is nonobvious, claim 12 which depends from claim 1, is also nonobvious. Thus, Applicants respectfully request that this rejection be withdrawn.

The Examiner also rejected claim 12 under 35 U.S.C. § 103(a) as allegedly being unpatentable under Okihara. The Examiner alleged that Okihara teaches the stereocomplex of the instant invention, except that Okihara is silent on the length of the monomers. Applicants must respectfully disagree, and address the Examiner's rejection in view of amended claim 1.

Okihara fails to teach or suggest claim 1, from which claim 12 depends from. As previously indicated, Okihara teaches crystalline complexes, which are not hydrogel compositions (*i.e.*, colloidal gels with water as a dispersion medium). There is no suggestion or motivation to

modify crystalline stereocomplexes to teach hydrogels, let alone hydrogels comprising non-covalent oligomeric groups of opposite chiralities. Because independent claim 1 is nonobvious, claim 12 which depends from claim 1, is also nonobvious. Thus, Applicants respectfully request that this rejection be withdrawn.

Finally, the Examiner rejected claims 15-17 under 35 U.S.C. § 103(a) as allegedly being unpatentable over De Jong *et al.* (*Macromolecules* 31: 6397-6402 (1998)) in view of Brannon-Pappas (*Int. J. Pharm.* 116: 1-9 (1995)). The Examiner alleged that De Jong discloses preparation of stereocomplexes from homopolymers or copolymers of D and L-lactides, and further discloses that stereocomplex formation is also observed in D and L-lactide/caprolactone blends. The Examiner admits that De Jong does not teach incorporating active ingredients in the stereocomplex. However, the Examiner alleged that it would be obvious to include an active ingredient in the hydrogel composition of De Jong since Brannon-Peppas teaches that lactide hydrogels can be drug carriers. Applicants must respectfully disagree.

To establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation to modify the reference or combine reference teachings. Second, the prior art reference (or references combined) must teach or suggest all the claim limitations. Finally, there must be a reasonable expectation of success should the modification or combination be carried out. MPEP 2143. As shown below, these requirements have not been met.

De Jong, either alone or in combination of Brannon-Pappas, fails to teach all the claim limitations in claims 15-17. Claims 15-17 relate to processes for preparing hydrogels by mixing two mixtures each comprising polymerized enantiomers coupled to a water soluble or water dispersible polymer. In contrast, De Jong is silent regarding hydrogels (*i.e.*, a colloidal where water is the dispersion medium) and water soluble or water dispersible polymers, let alone a process for preparing hydrogels by mixing two mixtures each comprising polymerized enantiomers coupled to a water soluble or water dispersible polymer. Instead, De Jong teaches the synthesis of lactic acid oligomers from heating a neat mixture of lactide and a compound with a primary hydroxyl group

such as 2-(2-methoxyethoxy)ethanol as initiator, and subsequent addition of stannous octoate as catalyst. (See De Jong, Synthesis of Polydisperse Methoxyethoxyethanol-Lactate (MEE-Lactate) at page 6398, and Results and Discussion at page 6399).

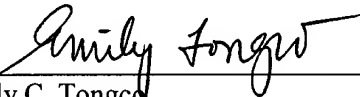
To remedy De Jong's failure to teach the preparation of hydrogels, the Examiner attempted to combine De Jong with Brannon-Pappas. However, Brannon-Pappas is also silent regarding hydrogels and water soluble or water dispersible polymers. Brannon-Pappas merely describes the use of biodegradable polymers in controlled drug delivery. Thus, even if De Jong and Brannon-Pappas were combined, the combination fails to teach a process for preparing hydrogels by mixing two mixtures each comprising polymerized enantiomers coupled to a water soluble or water dispersible polymer. Furthermore, since both references are silent regarding hydrogels and a process for preparing hydrogels, there is no reasonable expectation of success should the modification or combination be carried out. Based on the above, claims 15-17 are nonobvious. Thus, Applicants respectfully request that this rejection be withdrawn.

In view of the above, each of the presently pending claims in this application is believed to be in immediate condition for allowance. Accordingly, the Examiner is respectfully requested to withdraw the outstanding rejection of the claims and to pass this application to issue. If it is determined that a telephone conference would expedite the prosecution of this application, the Examiner is invited to telephone the undersigned at the number given below.

In the event the U.S. Patent and Trademark office determines that an extension and/or other relief is required, applicant petitions for any required relief including extensions of time and authorizes the Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to Deposit Account No. 03-1952 referencing docket no. 31363-2001000. However, the Commissioner is not authorized to charge the cost of the issue fee to the Deposit Account.

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Respectfully submitted,

By 
Emily C. Tongco

Registration No.: 46,473
MORRISON & FOERSTER LLP
3811 Valley Centre Drive, Suite 500
San Diego, California 92130
Tel: (858) 314-5413
Fax: (858) 720-5125